

551, 057

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
7 October 2004 (07.10.2004)

PCT

(10) International Publication Number
WO 2004/084831 A2

(51) International Patent Classification⁷:

A61K

(74) Common Representative: MERCK & CO. INC.; 126
East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

(21) International Application Number:

PCT/US2004/008677

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(22) International Filing Date: 19 March 2004 (19.03.2004)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/457,172

24 March 2003 (24.03.2003)

US

(71) Applicant (for all designated States except US): MERCK
& CO. INC. [US/US]; 126 East Lincoln Avenue, Rahway,
NJ 07065-0907 (US).

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), Euro-
pean (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR,
GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
ML, MR, NE, SN, TD, TG).

(72) Inventors; and

(75) Inventors/Applicants (for US only): JANSEN, Kathrin,
U. [DE/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-
0907 (US). SCHULTZ, Loren, D. [US/US]; 126 East Lin-
coln Avenue, Rahway, NJ 07065-0907 (US). NEPPER,
Michael, P. [US/US]; 126 East Lincoln Avenue, Rahway,
NJ 07065-0907 (US). MARKUS, Henry, Z. [US/US]; 126
East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

Published:

— without international search report and to be republished
upon receipt of that report

[Continued on next page]

(54) Title: OPTIMIZED EXPRESSION OF HPV31 L1 IN YEAST

HPV31 L1 total rebuild nucleotide and amino acid sequence:

```

1  M S L W R P S E A T V Y L P P V P
  A T G T C T T G T G A G A C A T C T G A A C T A C C G T C A C C A G T C C C
  51  V S K V V S T D E V Y T R T N I Y
  A B T C T C T A B G T G T C T C T A C C A G A T C C A C C A G A C A C A T C T
  101  Y H A G S A R L L T V G H P Y Y
  A C T A C C A C G C T G T T T G C T A G A T T G T T G A C C G T C A C C A T A C T A G
  151  S I P K S D N P K K I V Y P K V S
  T C T A T C C A A A G T C T G A C A C C A A G A G A G A T G T G T C C A G A G T C T C
  201  G L Q Y R V F R V R L P D P N K F
  T G T T T T G C A A T A C A G A G T C T C A G A G T C A G A T T G C A G A C C A A C A N E T
  251  G F P D T S F Y N F E T Q R L V
  T G G T T T T C C A G A C A C T C T T T C A C A C C C A G A A G C C A A G A T T G T C
  301  W A C V G L E V S R G Q P L G V G
  T G G C T T T G T G T G S T T T G S A A G T C G S T A G A G S T C A A C C A T T G G T S T C G G
  351  I S G H P L L N K F D D T E N S N
  T A T C T C T G T C C C C A C A T T G T G A C A G A T T C C A G A C A C C G A A A C T C T A
  401  R Y A G G P G T O N R E C I S H
  A C A G A T A C G C T G T T G T C T A C G T A C C A C A G A G A T G T A T C T C T A T G
  451  D Y K Q T Q L C L L G C K P P I G
  G A C T A C A G C A A C C A A T T G T T T T T G T G S T T A A G C C A C A A T G G
  501  E H W G K G S P C S N N A I T P G
  T G A C A C T G S G A T A G S G T T C T C A T A T T C T A C A A G S E T A T C A C C O G A
  551  O C P P L E L K N S V I Q D R D
  G T A C T G T C C A C C A T T G A A T T G A G A M E T C T G T A T C A C A G A C S T G A C
  601  N V D T G F G A N D F T A L Q D T
  A T G T G A C A C C G T T C G G T G T A T G A C T T C A C C G C T T T G C A A G A C A C
  651  K S M V P L D I C N S I C K Y P D
  C A G E T C T A C G T C C A T T G S A C A T C T G T A A C T A T C T G T A A G T A C C A G
  701  Y L K H V A E P Y G D T L F F Y
  A C T A C T T G A G A T G T G T C G E T G A N C A T A G S G E A C A C E T T G T C T C T A C
  751  L R R E Q M F V R H F F N R S G T
  T T G C T A G A G A A C A B A T E T T G S T A A G C A C T T C T T C A C A G A T C C G A C
  801  Y G E S V P T D L Y I K G S G S T
  G S T A G S T A A T C T T G T C C A A C C A C T G T A C A T A C A G S E C T G G T G T C A
  851  A T L A N S T Y F P T P S G S M
  C G G T A C C E T G E C T A A C T C C A C T A C T T C C A C T C A T C T G G T C C A T G
  901  V T S D A Q I F N K E P Y W H O R A
  G T C A C C T C G S A C E T C A B A T C T T C A C A A G C C A C A C T A G A T G A C G S T G C
  951  Q B H N N G I C V G N Q L F V T V
  A C A G S E T C A C A C A C G S T A T C T G T T G S G S Y A A C C A G C T G T T G T S T A C T G
  1001  V D T T R S T N N S V C A A I A
  T G T G S A T A C C A G S E T T C T A C A A C A T E T C T G T C T G T C T G C A T C E T
  1051  N S D T T F K S S H F K E Y L R H
  A A C T C T G A C C T A C C T T C A A G T C T C T A C A C T T A C A G A G A T A C C T G A G A C A
  1101  G E E F D L Q F I F Q L C K I T L
  T G S T G A G G A A T T G A T C T G C A A T C A T C T C A G T T G T G C A A G A T C A C C
  1151  S A D I N T Y I H S N R P A I L
  T G T C T G T G A C A T C A T G A C C T A C A T C A C A G A T A T G A C C T G C A T C T G C
  1201  E D V N F G L T T P S G S L E D
  G A S S A C T G S A A C T T G S T E T G A C A C T C A C C T T C G S E T T C T T T G A A G A

```

(57) Abstract: Synthetic DNA molecules encoding the HPV31 L1 protein are provided. Specifically, the present invention provides polynucleotides encoding HPV31 L1 protein, wherein said polynucleotides are free from internal transcription termination signals that are recognized by yeast. Also provided are synthetic polynucleotides encoding HPV31 L1 wherein the polynucleotides have been codon-optimized for high level expression in a yeast cell. The synthetic molecules may be used to produce HPV31 virus-like particles (VLPs), and to produce vaccines and pharmaceutical compositions comprising the HPV31 VLPs. The vaccines of the present invention provide effective immunoprophylaxis against papillomavirus infection through neutralizing antibody and cell-mediated immunity.

WO 2004/084831 A2



For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.